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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| In re application of: | : | | |
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| Lee, et al | : | Art Unit: 1636 | |
| | : | | |
| Serial No: | 10/534,433 | : | Examiner: Michele K. Joike |
| | | : | |
| Filed: | 21 November 2005 | : | Confirmation No. 5833 |
| | | : | |
| For: | DNA/RNA TRANSDUCTION TECHNOLOGY AND ITS CLINICAL AND BASIC APPLICATIONS | | |

DECLARATION UNDER 37 C.F.R. 1.132 OF Sang-Kyou Lee

VIA EFS
M/S AMENDMENT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1345

Sir:

I, Sang-Kyou Lee, declare and say as follows:

(1) I am a co-inventor of U.S. Application No. 10/534,433 ("the present application). At present, I am Professor of Biotechnology at Yonsei University, Korea. I hold a Ph.D. degree in Immunology, awarded by Yale University, U.S.A. Following this degree, I worked in Harvard Medical School Division of Immunology, as detailed in my attached Resume. As shown in my Resume, I am presently CTO in ForHumanTech Co. Ltd. Based on these facts, I consider myself, and believe my colleagues consider me, to be a person of skill in the art of Immunology, including in particular DNA/RNA transduction technology, such as that of the present application.

(2) The present application includes claims drawn to a method for delivering a biological regulator into eukaryotic cytoplasm or nucleus, comprising steps: i) Preparing peptide transducing recombinant expression vector which comprises a DNA encoding protein transduction domain(PTD), a DNA encoding one or more homologous or heterologous binding protein having DNA or RNA binding factor or DNA or RNA binding domain, and expression regulatory sequence operatively bound to the vector; ii) Obtaining a fusion protein by expression of the vector of step i) in a host cell; iii) Preparing a recombinant expression vector which comprises a DNA encoding a biologic

al regulator, a DNA or RNA binding sequence specifically binding to the DNA or RNA binding factor or the DNA or RNA binding domain, and expression regulatory sequence bound operatively to the vector; iv) Obtaining a binding complex by combining the fusion protein from step ii) with the recombinant expression vector from step iii); and v) Delivering the binding complex of step iv) into cytoplasm.

(3) It is my understanding that the claims of the present application have been rejected as obvious over Ye et al. in view of Zuckerman. I have carefully reviewed all of the references cited by the Examiner in rejecting the claims of the present application and the Examiner's rationale in support of the alleged obviousness.

(4) As a person of skill in the art, with all due respect, I cannot agree that the presently claimed invention as a whole would have been obvious to any person of ordinary skill in the art over the contended combinations of references according to the Examiner.

(5) In order to support my statements in paragraph (4) above, we have conducted a series of experiments, reported in the following paragraphs, which clearly show a significant effect on delivering a biological regulator such as DNA into a cell. Attached to this Declaration as Exhibit A is the results of FACS analysis to demonstrate the different results obtained by a process in accordance with the present invention as compared to the prior art.

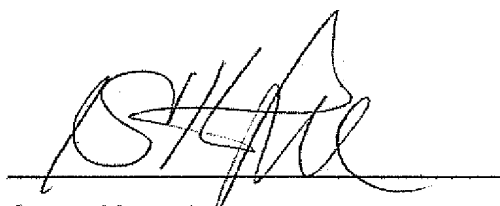
(6) Referring to Exhibit A, there are shown the result of FACS analysis. Lipofectamine is widely used for delivery of naked DNA. However, lipofectamine can not deliver the naked DNA into suspended cells such as T cells. In contrast, delivery using the method described in claims can deliver naked DNA regardless of cell type. pGFP(green fluorescence protein)-GBS(gal4 binding sequence), lipofectamine (Invitrogen) and Mph1-Gal4 were prepared, and primary T(CD3+) cells were extracted from rat spleen tissue. The complexes of lipofectamine-pGFP-GBS and Mph1-Gal4-pGFP-GBS(the present invention) were added to a 35mm Petri dish in which primary T cells (2×10^5) were incubated. After adding the complexes, the samples were incubated for 24hrs and the green fluorescence which was expressed by delivered pGFP was detected by FACS analysis.

(7) As shown by the foregoing and illustrated in the attached Exhibit A, the results demonstrate a clear and unexpected distinction between the prior art and the present invention. It is respectfully submitted that this evidence clearly shows that the combination described in the claims of the present patent application would not have been obvious when viewed against the prior art generally, and particularly when viewed against the prior art cited by the Examiner in the Office Action mailed from the U.S. Patent Office on 25 August 2009 and in the previous Office Action.

I, Sang-Kyou Lee, hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued therefrom.

Respectfully submitted,

10. Nov. 2009
Date


Sang-Kyou Lee

Curriculum Vitae



1) Personal Identification

- Name : Sang-Kyou, Lee
- Date of Birth : October 2, 1957
- Address : 2-503 HanGang Apartment Jamwon-Dong Seocho-Gu
Seoul, Korea

2) Educational Background

- 1976 ~ 1984 Yonsei University
 / Dept. of Biotechnology (B.S.)

- 1984 ~ 1986 Univ. of Michigan at Ann Arbor
 / Dept. of Microbiology and Immunology (M.S.)

- 1988 ~ 1992 Yale University, School of Medicine
 / Dept. of Immunology (Ph.D.)

- Graduation Thesis
 : Functional analysis of Ly-6A antigen and protein tyrosine kinase
Fyn in T cell activation. (Dr. Alfred Bothwell and Dr. Charles
Janeway)

3) Career

- 1992 ~ 1993 Harvard Medical School Division of Immunology
 (Postdoctoral Fellow)
- 1993 ~ 1995 Harvard Medical School Division of Immunology
 (Lecturer and Research Associate)
- 1995 ~ present Dept. of Biotechnology, Yonsei University
 (Professor)

- 1996 ~ present The Korean Association Immunobiologists (Director)
- 2000 ~ Present ForHumanTech Co.Ltd (CTO)

4) Publication

1. Lee, S.K.* , Su,B., Maher, S.E. and Bothwell, A.L.M. 1994 Ly-6A is required for T cell receptor expression and protein tyrosine kinase fyn activity. EMBO Vol. 13, 2167-2176
2. Lee, S.K.* , Shaw, A., Maher, S.E. and Bothwell, A.L.M. 1994 p59^{fyn} tyrosine kinase regulates p56^{lck} tyrosine kinase activity and early TcR-mediated signaling. International Immunology Vol.11, 1621-1627
3. Lee, S.K.* , Muller, B. and Terhorst, C.P. 1994 Specific interaction between the ectodomains of T cell Receptor CD3-ε and B cell Receptor B29. Immunology letters Vol. 57 45-52
4. Lee, S.K.* and Kim, Y.S. 1994 Physical and functional association of murine Ly-6 antigen with T cell Receptor complex. J. Immunol. Vol.16, 9-18
5. Wang, B., Biron, C., She,J., Lee,S.K.* , Sunshine, M.J., Lacy, E., Lonberg,N. and Terhorst C. 1994 A block in both early T lymphocyte and natural killer cell development in transgenic mice with high-copy numbers of the human CD3E gene. Proc. Natl. Acad. Sci. U.S.A. Vol.91 2778-2783
6. Levelt, N.C., Mombeerts, P., Lee, S.K.* , Kihoer,H., Tonegawa, S., Eichman, K. and Terhorts, C. 1995 Regulation of thymocyte development through CD3:Functional dissociation between p56^{lck} and CD3-ζ in early and late thymic selection. Immunity. vol.4 123-130

7. Jung-Hee Lim, Sang-Won kim, Young-Sup Song and Sang-Kyou Lee*. 1998 Tyrosine phosphorylation Independent Induction of Late Activation Events by Ig β signaling subunit of β cell receptor in Jurkat T cell. Immunology Letter Vol.61, 8-14
8. Sang-Won Kim and Sang-Kyou Lee*. 1998 Interaction of Vav with CD3-zeta upon T cell activation. BBRC. 252, 73-78
9. Sung-Ho Ha, Sang-Kyou Lee* and Tai-Hyun Park. 1998 Efficient Production of Recombinant Protein in Spodoptera Frugiperda/AcNPV system Utilizing Silkworm Hemolymph. BBRC, 250, 149-153
10. Tomohiro Morio, Silva H. Hanissian, Leonard B. Bacharier, Hirobumi Teraoka, Shigeaki Nonoyama, Makoto Seki, Jun Kondoh, Hiroyasu Nakano, Sang-Kyou Lee. Ku in the Cytoplasm Associates with CD40 in Human B Cells and Translocates into the Nucleus Following Incubation with IL-4 and Anti-CD40 mAb. Immunity, Vol. 11, 339-348, September, 1999
11. Jae-Hyuck Shim, Heung-Kyu Lee, Eun-Joo Chang, Wook-Jin Chae, Hyoung-Sik Chun, Duck-Jong Han Morio Tomohiro and Sang-Kyou Lee*. Immunosuppressive effects of tautomycetin in vivo and in vitro via T cell-specific Apoptosis Induction. Immunity (2001)
12. Wook-Jin Chae, Jin-Hwan Han and Sang-Kyou Lee*. Identification of Functional Domain in CD3-zeta for Initiation of T cell activation Submitted to Journal of Experimental Medicine (2001)
13. Jae-Hyuck Shim, Jae-Young Lee, Jin-Hwan Han, Wook-Jin Chae, Tomohiro Morio and Sang-Kyou Lee. The Intensity of Intracellular Activation Signals Determines Fas-mediated Activation-Induced Cell Survival or Death. Submitted to Nature Immunology (2001)

14. Gun-Soo Kim, Jin-Hwan Han and Sang-Kyou Lee. Regulation of the AP-1 Transcriptional Factor in Stably Transfected Jurkat T Cell Clones. Submitted to BBRC (2001)
15. "Immunosuppressive effects of tautomycetin in vivo and in vitro via T cell-specific apoptosis induction" PNAS / August 6, 2002
16. "The mutant leucine-sipper domain impairs both dimerization and Suppressive function of Foxp3 in T cells, PNAS / June 20, 2006
17. "Intra-nasal delivery of the cytoplasmic domain of CTLA-4 using a novel PTD prevents allergic inflammation", Nature Medicine / May , 2006